REMARKS

After entry of the amendments made herein claims 1-14 and 16-28 are pending in the application. Claim 20 is allowed. Claims 1-13 and 15-19 are withdrawn from further consideration as being drawn to a non-elected invention. Claim 15 is herein cancelled. New claims 21-28 are herein added. New claim 27 is based on original claim 15 and is drawn to a method utilizing the immunoglobulin molecule of allowed claim 20. Claim 27 includes all limitations of allowed claim 20 and thus, Applicants request the Examiner allow claim 27. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s). The amendment finds support in the specification and is discussed in the relevant section below. No new matter is added.

Applicant thank Examiner Sims for withdraw of the rejection of the claims under 35 U.S.C. §103 and allowance of claim 20.

Rejection of the claims under 35 U.S.C. §112

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Action states that the claims contain subject matter which was not described in the specification in such a way as to enable on skilled in the art to make and/or use the invention. Specifically, the Action alleges that undue experimentation is required to practice the claimed invention which is directed to intracellularly binding immunoglobulin molecules having a variable heavy chain which exhibits at least 95% homology to the consensus sequence of SEQ ID NO:3.

Applicants respectfully traverse the rejection.

Claim 14 is directed to an intracellular binding immunoglobulin molecule with a variable heavy chain which exhibits at least 95% homology to the consensus sequence SEQ ID No 3. New dependent claim 21 requires that the immunoglobulin of claim 14 specifically binds BCR or BCR-ABL. Support for this new claim can be found on throughout the application as filed including, paragraph 252 of the corresponding US

Publication No. 2005/0288864 (herein the Publication), FIG 5 and the corresponding brief description of FIG 5, Example 6 and Example 7. New dependent claims 22-25, further require that the immunoglobulin of claim 21 has a variable heavy chain which exhibits at least 96%, 97%, 98%, and 99% homology, respectively, with the consensus sequence of SEQ ID NO:3. Support for new claims 22-25 is found throughout the application including paragraph 96 of the Publication. New claim 26 requires that the intracellularly binding immunoglobulin of claim 21 has three complementary determining regions having amino acid residues 27-35, 50-66 and 99-101 of SEQ ID NO:3. Support for this claim amendment can be found thought the specification and in particular in FIG 5A and the corresponding brief description of FIG. 5A (paragraph 152 of the Publication).

In *In re Wands*, the court stated that "[e]nablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is 'undue' not 'experimentation' (citing *In re Angstadt*, 537 F. 2d 498 at 504, 190 U.S.P.Q. 214 at 219 (C.C.P.A. 1976)). The Court also stated that "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." (citing *In re Jackson*, 217 U.S.P.Q. 804 at 807 (Bd. App. 1982)), emphasis added.

The specification provides ample guidance for producing intracellular immunoglobulin molecules that have a variable heavy chain comprising an amino acid sequence that is 95% or more identical to SEQ ID NO:3. For example, art-accepted techniques for producing and screening these immunoglobulin variants can be found in paragraphs 185-204 and 237-245 of the Publication. Thus, the specification fully enables the production and use of intracellular immunoglobulins which have a variable heavy region that is 95% identical with SEQ ID NO:3.

Furthermore, the present application describes many species of intracellular immunoglobulins having variable heavy chains which differ from the consensus sequence of SEQ ID NO:3 yet bind BCR. Sequence alignments of these variable heavy chain polypeptides with SEQ ID NO:3 are illustrated in Fig. 5A. The sequences (SEQ ID NOs: 5-22) exhibit multiple mutations in both the framework and CDR regions. In fact, many of these sequences have less than 95% identity with SEQ ID NO:3 yet still bind BCR. The application teaches that these variant heavy chain sequences are able to bind BCL in vitro (FIG. 2) and in vivo (FIG. 3).

In support of the unpredictability of antibodies the Action references Chiba et al. stating that "a particular amino acid substitution on Leu3a binding activity is often ***somewhat*** unpredictable." [emphasis added]. Applicants disagree that Chiba et al. supports a finding of unpredictability so as to render the claimed invention invalid for lack of enablement. The Wands factors must be looked at as a whole not in isolation. Applicants believe that Chiba et al. teaches that making and using variant species of antibodies is predictable. As the Action acknowledges, Chiba et al. states that "key residues may be readily **substituted without sacrificing biological activity**." [emphasis added] Thus, Chiba et al. teaches in fact that there is a good degree of predictability that would not require undue experimentation to make and use the intracellular immunoglobulin molecules having variable heavy chains which are at least 95% identical to SEQ ID NO:3.

Furthermore, in *Ex parte Kubin* [Appeal No. 2007-0819, May 31, 2007 (BPAI)], the Board of Patent Appeals and Interferences held that undue experimentation is not required to practice the full scope of a claim reciting DNA encoding polypeptides "at least 80% identical" to a reference polypeptide. The Board examined the Wands factors and concluded that while "molecular biology is generally an unpredictable art . . . the other Wand's factors weigh in Appellants' favor, particularly 'the state of the art' and 'the relative skill of those in the art.'" See *Ex parte Kubin* at page 14. Moreover, the Board cited both Johns Hopkins Univ. v. Cellpro, Inc. (Fed. Cir. 1998) and Hybridtech Inc. v. Monoclonal Antibodies. Inc. (Fed Circ. 1986) to re-emphasize that even though

extensive experimentation was needed to obtain active variants, it was nevertheless merely routine. Id. At 14-15. Accordingly, the instant rejection is at odds with the Board's determination that protein variants up to 80% identical to a reference protein could be practiced by one of skill in the art without undue experimentation.

In view of the teachings in the specification, knowledge in the art and the *Ex parte Kubin* decision, Applicants submit that all claims are fully enabled. Accordingly applicants respectfully request that the rejection of claim 14 under 35 U.S.C. §112, first paragraph for alleged lack of enablement be reconsidered and withdrawn.

CONCLUSION

In light of the above remarks, Applicants respectfully request early consideration and allowance of the subject application.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

The Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment to Deposit Account No. 04-1105.

Respectfully submitted,

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